

### REMARKS

Upon entry of this amendment, Claims 34, 36 and 37 are pending in this application. Claims 1-33, 35, and 38-50 are canceled without prejudice to Applicants' right to pursue the subject matter of these claims in a related application.

#### Election/Restriction

In response to the restriction requirement, Applicants have amended the claims to specifically recite PD098059 as the second compound.

#### Drawings

In view of the Examiner's indication that the drawings cannot be added to the application in spite of the extensive description of those drawings contained in the specification, Applicants have amended the specification to delete reference to the drawings.

#### Claim Objections

The claims as amended overcome the Examiner's objections.

#### 35 U.S.C. § 112, first paragraph

The claims as amended are fully supported by the application as filed and comply with the written description and enablement requirements of 35 U.S.C. §112, first paragraph. Issues raised by the Examiner in connection with canceled claims are considered moot.

In the final Office Action, the Examiner suggests that the "limitation of 'dissociating the cells' and 'maintaining the dissociated cells' in claims 34 and 37 are new matter and lack written description." (Office Action at p. 11.) Applicants respectfully submit that the Examiner is mistaken. Original claim 35 recited both steps of "dissociating the cells" and "maintaining the dissociated cells." Further support for the recited steps can be found in Example 2 of the specification (page 27, lines 8-12). Example 2 states that epiblasts were isolated and then maintained in culture in the presence of P098059. The epiblasts were then dissociated and the dissociated cells were maintained in culture in the presence of PD098059. Consequently, both claims 34 and 37 are fully supported by the application as filed.

The Examiner also contends that "the limitation of developing an embryo in vitro (claim 37) is new matter." (Office Action at p. 11.) As Applicants noted in the last response, because this language was part of the original claim, it cannot be considered new matter.

Claims 34, 36 and 37 stand rejected as allegedly failing to comply with the enablement requirement of 35 U.S.C. §112, first paragraph. (Office Action at p. 12.) In the final Office Action, the Examiner contends that the claims are not enable because the specification does not teach how to generate the genetically altered ES cells used as the starting material in the assays described.

Applicants previously argued that the constructs used to exemplify the methods of the invention are of a type known in the art. The Examiner correctly notes that U.S. Patent 6,150,169, relied upon by applicants was not available to the public until two years after the effective filing date of the present application. However,

WO 94/24301, the international application on which that U.S. patent was based, was published on October 27, 1994. Thus, before the filing of the present application, sufficient detail of how to make constructs of the type used in the claimed invention was provided in WO 94/24301.

The application as filed explains, e.g., that beta-galactosidase was expressed from the Oct 4 locus – see page 18, first 2 lines. This makes clear that the Oct 4 promoter drives expression of the beta- galactosidase transgene. This disclosure, in combination with Mountford et al. (previously submitted) and WO 94/24301, is sufficient for a person of skill in the art to make the construct.

It should be noted that the examples were carried out to confirm to the inventors' satisfaction that LIF and PD 098059 enhanced self-renewal of ES cells and that this observation was not attributable to other factors. The invention claims that a combination of LIF and PD098059 can be used to culture ES cells with increased self-renewal of those ES cells. To carry out the invention a skilled person need only culture ES cells in LIF and PD098059. The skilled person need not repeat the proof of principle work carried out by the inventors which the inventors deemed necessary before the inventors were prepared to declare their invention to the public.

Moreover, it is not necessary to use genetically modified ES cells for the invention to work. As noted above, these constructs were used to test the principles of the invention and confirm the effects were attributable to LIF and PD098059 rather than to other factors. The invention will in practice be carried out on genetically altered ES cells but also, and more preferably, on ES cells that have not been genetically altered.

Applicants draw the Examiner's attention to the following references which identify ZIN40, DO27 and IOUD2 cells as ES cells: Charriere et al., Abstract from NCBI, sample GSM26334 (ZIN40); Abstract from Physiology Image Gallery (IOUD2); and Niwa et al., Genes and Development, 12(13): 2048-2060 (1998) (DO27). Copies of these references were provided to the Examiner with the last response.

Applicants respectfully submit that the amended claims are fully enabled and request that the rejection under 35 U.S.C. § 112, first paragraph, be withdrawn.

35 U.S.C. § 112, second paragraph

Applicants submit that the amended claims obviate the rejections under 35 U.S.C. § 112, second paragraph.

In view of the foregoing amendments and remarks, Applicants respectfully request reconsideration and reexamination of this application and the timely allowance of the pending claims.


Please grant any extensions of time required to enter this response and charge any additional required fees to deposit account 06-0916.

Respectfully submitted,

FINNEGAN, HENDERSON, FARABOW,  
GARRETT & DUNNER, L.L.P.

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By:

  
Leslie A. McDonnell  
Reg. No. 34,872